

CLAIMS:

Sub
C1
1. An assay method for a compound able to modulate the interaction or binding between XRCC4 and DNA ligase IV, or
5 XRCC4 and DNA-PK_{CS}/Ku, or XRCC4, DNA ligase IV and DNA-PK_{CS}/Ku, the method including the steps of:

(a) bringing into contact a substance including XRCC4 or a peptide fragment of XRCC4 or a derivative, variant or analogue thereof able to bind DNA ligase IV or DNA-PK_{CS}/Ku, a
10 substance including DNA ligase IV or a peptide fragment of DNA ligase IV or a variant, derivative or analogue thereof able to bind XRCC4 and/or including DNA-PK_{CS}/Ku or a peptide fragment of DNA-PK_{CS}/Ku or a variant, derivative or analogue thereof able to bind XRCC4, and a test compound, under
15 conditions wherein, in the absence of said test compound being an inhibitor of interaction or binding between said substances, said substances interact or bind; and

(b) determining interaction or binding between said substances.

20
2. An assay method for a compound able to modulate interaction or binding between XRCC4 and DNA ligase IV or XRCC4 and DNA-PK_{CS}/Ku, or XRCC4, DNA ligase IV and DNA-PK_{CS}/Ku, the method including the steps of:

25 (a) bringing into contact a substance including XRCC4 or a peptide fragment of XRCC4 which interacts with DNA ligase IV or DNA-PK_{CS}/Ku, or a derivative, variant or analogue thereof which interacts with DNA ligase IV or DNA-PK_{CS}/Ku, or which includes DNA ligase IV or DNA-PK_{CS}/Ku or a
30 peptide fragment of DNA ligase IV or DNA-PK_{CS}/Ku which interacts with XRCC4, or a derivative, variant or analogue thereof which interacts with XRCC4, and a test compound; and
(b) determining interaction between said substances and the test compound.

3. An assay method for a compound able to affect DNA ligase IV activity, the method including the steps of:

(a) bringing into contact DNA ligase IV and a test compound; and

5 (b) determining DNA ligase activity.

4. An assay method according to claim 3 wherein the DNA ligase activity is determined in the presence of XRCC4.

Sub 2
10 5. An assay method according to ^{claim 4} ~~3 or 4~~ wherein the activity of DNA ligase is determined by its adenylation or labelling by using an ATP analogue, or ability to join strands of DNA or DNA analogues.

15 6. An assay method including

(a) bringing into contact a substance which includes DNA-PKcs/Ku or suitable peptide fragments of DNA-PKcs/Ku or derivative, variant or analogue thereof able to phosphorylates XRCC4, a substance which includes XRCC4 or a peptide fragment of XRCC4 or a derivative, variant or analogue thereof including a site phosphorylated by DNA-PKcs, and a test compound; and

(b) determining phosphorylation at said site.

25 7. An agent capable of modulating interaction between XRCC4 and DNA ligase IV, or XRCC4 and DNA-PK_{CS}/Ku, or XRCC4 and DNA ligase IV and DNA-PK_{CS}/Ku, obtained using a method according to claim 1 or claim 2.

30 8. A peptide fragment of DNA ligase IV capable of modulating interaction between XRCC4 and DNA ligase IV, or XRCC4 and DNA ligase IV and DNA-Pk_{CS}/Ku.

9. A peptide according to claim 8 which has a sequence
35 found in human DNA ligase IV between amino acid residues

591-676 using the numbering of Wei, et al., (1995). *Mol. Cell. Biol.* **15**, 3206-3216.

10. A peptide according to claim 8 which has a sequence 5 found in human DNA ligase IV between amino acid residues 728-844 using the numbering of Wei, et al., (1995). *Mol. Cell. Biol.* **15**, 3206-3216.

a 10 11. A peptide according to claim 8 which has a sequence found in human ~~DNA Ligase IV~~ ^{DNA Ligase IV} between amino acid residues 677-727 using the numbering of Wei, et al., (1995). *Mol. Cell. Biol.* **15**, 3206-3216.

12. A nucleic acid isolate encoding a peptide according to ~~any one of claims 8 to 11~~ ^{claims 8}.

13. A peptide fragment of XRCC4 capable of modulating interaction between XRCC4 and DNA ligase IV.

20 14. A nucleic acid isolate encoding a peptide according to claim 13.

15. An agent able to affect DNA ligase ^{IV} activity obtained using a method according to any one of ~~claims 3 to 5~~ ^{claim 3}.

25 16. An agent able to affect DNA-PKcs/Ku phosphorylation of XRCC4 obtained using a method according to claim 6.

30 17. An agent or peptide fragment or nucleic acid isolate according to any of claims 5 to 16 for use in a method of treatment by therapy involving modulating cellular DNA repair activity.

18. Use of an agent or peptide fragment or nucleic acid

isolate according to any of claims 5 to 16 in the manufacture of a medicament for modulating cellular DNA repair activity.

Sub C3
5 19. A method which includes, following obtaining a compound able to modulate the interaction or binding between XRCC4 and DNA ligase IV, or XRCC4 and DNA-PK_{CS}/Ku, or XRCC4 and DNA ligase IV and DNA-PK_{CS}/Ku, employing a method according to claim 1 or claim 2, formulating the compound into a
10 composition including a pharmaceutically acceptable excipient.

20 20. A method which includes, following obtaining a compound able to modulate the interaction or binding between XRCC4
15 and DNA ligase IV, or XRCC4 and DNA-PK_{CS}/Ku, or XRCC4 and DNA ligase IV and DNA-PK_{CS}/Ku, employing a method according to claim 1 or claim 2, providing the compound to a cell to modulate cellular DNA repair activity.

20 21. A method according to claim 20 wherein the cell is not part of a human or animal body.

Sub C4
a
22. A method which includes, following obtaining a compound able to affect DNA ligase IV activity employing a method
25 according to ~~any one of claims 3 to 5~~, formulating the compound into a composition including a pharmaceutically acceptable excipient.

a
23. A method which includes, following obtaining a compound
30 able to affect DNA ligase IV activity employing a method according to ~~any one of claims 3 to 5~~, providing the compound to a cell to modulate cellular DNA repair activity.

24. A method according to claim 23 wherein the cell is not
35 part of a human or animal body.

Sub
15

25. A method which includes, following obtaining a compound able to affect DNA-PKcs/Ku phosphorylation of XRCC4 employing a method according to claim 6, formulating the compound into a composition including a pharmaceutically acceptable excipient.

26. A method which includes, following obtaining a compound able to affect DNA-PKcs/Ku phosphorylation of XRCC4 employing a method according to claim 6, providing the compound to a cell to modulate cellular DNA repair activity.

27. A method according to claim 26 wherein the cell is not part of a human or animal body.

28. A method for screening an individual for a predisposition to a disorder in which DNA repair plays a role, the method including determining from a sample taken from the individual the presence or absence of a defect in XRCC4 and/or DNA ligase IV activity.

562720-5054E50